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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,744	07/20/2000	HISAYOSHI SHIMIZU	2501US0P	1419

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EXAMINER
PULLIAM, AMY E

ART UNIT	PAPER NUMBER
1615	18

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/600,744	Applicant(s) SHIMIZU ET AL.	
	Examiner Amy E Pulliam	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10,13,14 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10,13,14 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Extension of Time, Request for Reconsideration, and Declaration, all received by the Office March 12, 2003.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, and 8, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 394 050 A2 to Ueda *et al.*. Ueda *et al.* disclose a method of preparing a freeze dried preparation in which a first liquid is frozen, a second liquid is added to the frozen first liquid, and the frozen first and second liquids are freeze dried together, wherein one of the two liquids contains a pharmaceutically active compound or a preparation dissolved or suspended therein (p 11, claim 1). Ueda *et al.* further teach that the process takes place in a container (p 4, l 11). Claim 9 of the reference teaches that the liquids are frozen at temperatures of between –10 and –50°C. Example 5 of reference 1 teaches applicant's method of coating the inside of a container (vial) with ice, and then proceeding with the freeze drying steps. The teachings of Ueda *et al.* anticipate the limitations of applicant's above listed claims.

Applicant's arguments filed March 12, 2003 have been fully considered but are not found to be persuasive. Applicant argues that the previously filed Declaration clearly differentiates the instant claims from the cited prior art. Applicant has submitted a similar, but more detailed Declaration, in an effort to more clearly persuade the examiner. The declaration contains experiments, which are asserted to be comparative experiments between applicant's claimed method and the method of the cited prior art. Upon careful examination of the experiments, the examiner notes that the only difference between the two experiments is that Example 1 uses mannitol, while example 2 uses "microcapsule powder." Otherwise, there are no differences between the two experiments. The examiner stated in the previous office action that it was not clear what applicant is using as the "microcapsule powder." This is troubling because it appears the particular material used is of great importance being that it is the variable which differs in the two experiments. Applicant responded to this argument by pointing to page 1, lines 12-19 of the specification, where Applicant asserts that microcapsule powder is defined. This passage has only caused further confusion, as "microcapsule powder" appears to be the final product which is obtained after the claimed method. More specifically, the above cited passage states, "... which is then dehydrated and dried by freeze-drying to yield a finished microcapsule powder." Therefore, using this definition makes Applicant's declaration more unclear, as the substance being added to the ice lined container is the finished product of the process itself. This is obviously not what was intended by the Declaration, however, exactly what was meant by the Declaration remains unclear.

For the above reasons, the examiner reasserts her objections made in the prior office action. First, as stated above, the only difference between the experiments in the declaration is

that Example 1 uses mannitol, while example 2 uses "microcapsule powder." Otherwise, there are no differences between the two experiments. It remains unclear what applicant is using as the "microcapsule powder." This is troubling because it appears the particular material used is of great importance being that it is the variable which differs in the two experiments. Second, it appears that any differences between the two examples are due to the specific material, however, no specific material is stated in either the claims or the declaration. More specifically, if applicant's asserted unexpected results are due to the use of a particular material, then this particular material must be included as a claim limitation. As currently stated, applicant's generic claim is very broad, and remains anticipated by the teachings of Ueda *et al.*.

Applicant states that the comparative results and photographs submitted in the Declaration clearly show that when the production method is applied for microsphere suspension, there is no undesirable scattering of the preparation. Applicant asserts that in contrast, if the method is run using an aqueous solution of a hydrophilic compound, then a large amount of scattering occurs. Unfortuantely, this argument is not found persuasive. It is clearly stated in the above rejection that the cited reference teaches that the active agent may be suspended or dissolved. It appears that Applicant is really trying to differentiate from the prior art by stating that Applicant requires a suspension while the prior art requires a solution. This is simply not true, as is stated in the above rejection. For these reasons, the above rejection is maintained.

Additionally, applicant has attempted to make the scope of the declaration commensurate with the scope of the claims by using the generic term "microcapsule powder" in the declaration. However, obviously a specific material was used in Experiment 2. This particular material needs

to be stated in the Declaration. However, this then creates a problem, because the declaration is no longer commensurate in scope with the generic claims, once a particular material has been inserted. This discussion is to demonstrate to applicant that the instant declaration is not supportive of the very broad claims currently pending. Applicant has asserted an unexpected result using one particular material instead of mannitol (even though that particular material is not stated in the declaration). This assertion does not extrapolate to any and all materials used in the formation of microspheres and microcapsules. It is recommended that applicant do one of two things. 1) More detailed limitations should be added to the claims, to more specifically state applicant's invention. For instance, what is it that makes applicant's claimed process different than the process of the prior art. Right now, the claims do not contain any such limitations. 2) Submit a more extensive declaration, which is commensurate in scope with the claims. If a new declaration is submitted, it is recommended that applicant include more detailed data, such as discussion of how the scattering is observed, and a statistical analysis of this data to demonstrate if the differences are significant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8, 10, 13, 14, 16, and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 394 050, as discussed above, and in view of the following comments.

Ueda *et al.* do not specifically teach that the resultant product be microcapsules. However, it is the position of the examiner that the process of freeze drying is well known in the art. This process results in a porous sheet at the bottom of the freeze drying contained. Upon scraping the sheet, a powder is formed. It is the position of the examiner that there is no patentable distinction between the resultant product of applicant and the resultant product of the cited art. Furthermore, the Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Ueda *et al.* do not specifically disclose a layer of a water repelling substance. However, Ueda *et al.* do teach the used of at least two frozen layers of different liquids (p 3, l 55-57). Based on the generic teachings of Ueda *et al.*, one of ordinary skill in the art would have been motivated to perform the freeze drying process by lining a container (such as a vial) with ice, and an additional layer of a different liquid, and then proceeding with the freeze drying steps. There are no limitations in Ueda *et al.* as to what the second liquid may be. However, Ueda *et al.* do teach that one of the layers contains a pharmaceutical active suspended or dissolved therein (p 3, l 35-36). Therefore, it is the position of the examiner that if the desired active for the formulation is a hydrophobic active, then the skilled practitioner would use a hydrophobic layer

in addition to the ice layer. If the desired active for the formulation is hydrophilic, the skilled practitioner could place the active in the water-ice layer, or use a hydrophilic liquid as the second layer. Either way, one of ordinary skill in the art would have been motivated to use either a hydrophobic or hydrophilic layer as the second layer to be frozen in the container. The expected result would be a pharmaceutically acceptable lyophilized formulation.

Additionally, the purpose of applicant's claimed invention it to supply a process with a better yield of microcapsules, with a reduced risk for entry of foreign substances. These are the same problems addressed in the Ueda *et al.* disclosure. Ueda *et al.* teach that their invention overcomes problems such as contamination, as well as faster and better recovery (p 3, l 1-35). Therefore, absent any evidence to the contrary, applicant's claimed invention achieves the same goal as that of the prior art, with no unexpected results. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been considered but are not found to be persuasive. Applicant's arguments have been discussed above and no further response is deemed necessary.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A. Pulliam
Patent Examiner
Art Unit 1615
May 27, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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